Featured Report on a Landmark Study

Dr. Simpson Comes to Gloucestershire

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Our understanding of the relative contagiousness of various common infectious diseases is derived from several sources: a few deliberate studies, such as planned ingestion of known inocula of salmonella or shigella[1]; "accidents of nature" wherein an outbreak of tuberculosis,[2] measles,[3] or the like, leads to an improved understanding of a known principle of transmission or elucidation of a new one; or retrospective, often community- or hospital-based prevalence studies, where a team of researchers delineates the extent of a specific disease. Examples of the latter include studies of tuberculosis,[4] hepatitis B,[5] and the childhood viral exanthems,[6,7] including measles, mumps, and chickenpox.

Many of the latter type of community- or hospital-based studies are now decades old and long-ago entered standard texts as "the facts of life." Everyone, for example, is aware that varicella virus is extremely contagious, more so than diseases such as tuberculosis. The studies that led to this now seemingly self-evident truth however, are long forgotten. A review of two seminal studies demonstrating the contagiousness of chickenpox and other childhood illnesses is immensely instructive, demonstrating both the quality and the keenness of the observations as well as the painstaking work that went into each.[6,7] Pox were counted, families and primary physicians interviewed and prodded, and cautious conclusions made.

R. E. Hope Simpson conducted a landmark study, "Infectiousness of Communicable Diseases in the Household (Measles, Chickenpox, Mumps)," and established and confirmed certain rules of thumb that guide current infectious disease and infection control practitioners.[6] The study was performed in Gloucestershire, a semirural town of some 11,000 inhabitants, as well as the surrounding agricultural area. Complete records were kept over 4 years, from June 1, 1947, to May 31, 1951. Members of the epidemiologic research unit, including Dr. Simpson, visited the town frequently, confirming each diagnosis with great care, thus ensuring the quality of the data. This was particularly important for a purely clinical study such as this one, done prior to the availability of serologic tests. As Dr. Simpson noted, "Approximately accurate data, though useful for certain purposes, can be most damaging when associated with more accurate data for other purposes."

In addition, because the study sought to distinguish primary transmissions from secondary transmissions in households, timing of onset of each of the three diseases of interest was crucial. Dr. Simpson's team developed conservative "points of measurement" for each disease (conjunctivitis, start of rash, maximum rash, etc.) and employed these definitions throughout the study, going as far as to review all primary physicians' records, to speak to each family member as well as the patient, and so on, until exact dates could be established.

Dr. Simpson's findings are shown in Table 1. For each of the three diseases, about 300 susceptible persons, 250 younger than 15 years of age, and 50 over 15 years of age were identified, and a slightly larger number of exposures identified, since some persons had more than one exposure. The attack rates in those younger than 15 years for each disease (transmissions/exposures) were 75.6% for measles, 61% for varicella, and 31.1% for mumps. Dr. Simpson chose to split the group into those younger and those older than 15 years because of the apparent disparity of the results. The lower attack rates for the older age groups was presumed to be due to the "fading memory of childhood illness." Current understanding of the diseases would also allow for a certain percentage of cases

Table 1. Infectiousness: Exposure Attack-Rate among Susceptibles in the Home

Age-Group	*Measles*	*Varicella*	*Mumps*
Contacts 0–15 years of age			
Susceptibles	251	238	218
Exposures	266	282	264
Transmissions	201	172	82
Escapes	65	110	182
Exposure attack-rate	75.6%	61.0%	31.1%
Contacts >15 years of age			
Susceptibles	36	64	96
Exposures	47	100	125
Transmissions	7	12	43
Escapes	40	88	82
Exposure attack-rate	14.9%	12.0%	34.4%
Mean age of infection (yr)	5.6	6.7	11.5
Age that 90% of cases have occurred (yr)	8.3	10.7	29

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of subclinical disease as well as those clinical diseases subsequently forgotten.

To further emphasize the tenets of transmission, Dr. Simpson next considered the mean age of infection, stating that "the more infectious the disease, the younger is the age at which an attack is likely to be received." In this analysis as well, mumps was significantly less transmissible than the other two diseases, with the mean age of transmission at about 12 years, versus the 6 years seen with varicella and measles.

Subsequent studies confirmed Dr. Simpson's careful work. In 1962, Ross and colleagues reported on chickenpox transmission in 773 children in 318 families in East Meadow, New York, and made similar conclusions.[7] Among these children, 322 primary cases of chickenpox occurred. In a study to determine the efficacy of gamma globulin, the 451 uninfected children were then randomized to receive or not receive gamma globulin. Of the 209 randomized to placebo, 182 (87%) went on to develop chickenpox (the same rate as occurred in those receiving gamma globulin). Among those who escaped infection at first exposure but were re-exposed to a family member who had become a secondary case, 71% developed chickenpox, yielding a combined attack rate (secondary and tertiary cases) of 96%, a rate higher than that noted by Dr. Simpson, a continent and a decade away. The rate determined by Ross and colleagues is the one typically given in textbooks. Ross also was able to demonstrate that secondary cases occurred in younger children (3-year-olds versus about 6-year-olds for primary cases) and were associated with about 50% more pox.

Current transmission studies increasingly have relied on seroprevalence of antibody in a community and, more recently, on gene-based techniques to elucidate the molecular epidemiology of a given disease. However, as more is learned about disease transmission, it is important to recall these older trials, complete with vast scale (an entire town), shrewd study designs, often formal language, and elemental conclusions, for from these works has come the bulk of what is known about disease transmission. Recent work has only served to refine and confirm the works of observers such as R. E. Hope Simpson.

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